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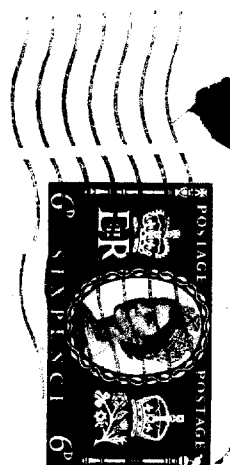
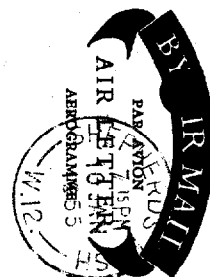
DUCANE ROAD
LONDON W.12

10 January, 1955.

Dear Joshua,

Many thanks for your letter and the interesting report of your recent work. I didn't mind a bit not getting it in time for our colloquium. I would not have produced it anyway unless you especially wished it. One usually begins by intending to tell as much as you can about everything, but finds, in the issue, that limitations of time demand a rather frightening dogmatism. Sorry to have misunderstood you about your interest in my phage work. We now go a long way together and I am a firm supporter of conjugation, which I have advocated to many people, officially and unofficially, during the past year. I am sure that the streptomycin technique works only because it does not kill the F⁺ cell rapidly; in fact I would attribute the usual marked drop in fertility of S-treated F⁺ cells ~~as due~~ to killing. This, of course, in no way affects the theoretical implications as to one-way transfer, which I now take to be more or less proven. I appreciate your substantiation. When taken in conjunction with the arguments you have put forward from time to time in favour of fusion, my views were re-orientated by two findings: 1) the fact that the T phages, which really do kill cells, abolish the fertility of F⁺ & Hfr cells very rapidly, and 2) that asparagine or aspartate or succinate &c. appear to be necessary for zygote formation. When mixtures of F⁺ + F⁻ or Hfr + F⁻ are plated on appropriate minimal media solidified with highly purified agar or with silica gel, there is virtually no recombination. When aspartate, but not glutamate or any other amino acid tried, is added however, the recombination rate rises to a much higher level than I had previously encountered: but prototrophs, or zygotes which have been "preformed" in broth, grow and segregate respectively on the medium without aspartate. At present I have rather a good Ph.D. student working on this and trying to elucidate the mechanism. I have now taken the kinetics of segregation rather further and in more detail (see my last letter) and find there is probably a lag of several divisions before recombinants become phenotypically expressed - at any rate so far as phage resistance is concerned. I was particularly interested in para. 3 of p. 5 of the report you sent me. I have also, by an indirect method, come to the conclusion that the higher fertility of Hfr strains is due to the much higher frequency of conjugations. If equal numbers of young Hfr & F⁻ cells are mixed in broth at population densities of about $3-5 \times 10^8$ /ml., aerated at 37° and viable counts done at intervals, there is no increase in numbers of either.

parent for at least two hours. If, however, the Hfr parental culture (or vice versa) is mixed with the centrifuged supernatant of the F- culture or with the F- culture heated at 56° for 10-15 mins., normal multiplication occurs as compared with the control. This is a very striking phenomenon and is not seen with F+ + F- or F- + F- cultures. It is my intention to try to analyse it in morphological terms when I get the microscope which has been promised me. I got quite excited about Jinks' exposé of his and Cavalli's work on the position of the E locus and the effects of imperfect pairing. If, as they (& you in relation to the diploids) suggest, inheritance of the E locus (or loci) is responsible for elimination, the reciprocals of the presumptively eliminated prototrophs should be found at high frequency in Hfr x crosses. It is not clear to me whether polymyxin resistance, which they place at the opposite end of the chromosome to (TL), is really a single step mutation, but if it is it should serve as a good selective marker in complete media to test this. As you see I have now come a long way with you. I am still worried, though, about the multiple functions of F. Its "eliminator" function may well be analogous to that of the lambda prophage locus, but how does it determine one-way transfer, is this quite irrelevant so far as inheritance is concerned? if it is like a temperate phage which cannot lyse the cell in the vegetative stage, its high rate of infectivity at conjugation presumes that it behaves constantly as a cytoplasmic particle. It is all very fascinating. If you were invited to speak at a symposium on bacterial genetics in London next year or the following, expenses paid, would you come? Best wishes for the new year to you both. *Bella*



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